

## CLAIMS

I claim:

1. A system for radiographic imaging of body tissue comprising:
- a cell membrane-permeable, radio-opaque imaging agent;
  - means for administering said imaging agent to a patient;
  - means for generating a plurality of X-ray beams with predetermined different energy spectra;
  - means for acquiring radiographic images disposed on the side of said patient opposite said X-ray beam generating means; and
  - means for performing a weighted combination of a plurality of said radiographic images to produce a single image.
2. The system of claim 1 wherein said plurality of beams are quasi-monoenergetic.
3. The system of claim 1 wherein said plurality of beams are monoenergetic.
4. The system of claim 1 wherein 2 beams are generated.
5. The system of claim 1 wherein more than 2 beams are generated.
6. The system of claim 1, further including means for displaying variable proportions of radiographic density contributed by said imaging agent, soft tissue, and bone to said single image.
7. The system of claim 1 wherein said cell membrane-permeable, radio-opaque imaging agent selectively binds to a cellular target.

8. The system of claim 7 wherein said cellular target is a cellular structure.
9. The system of claim 7 wherein said cellular target is a molecule.
10. The system of claim 7 wherein said cellular target is selected from the group of proteins, nucleic acids, coenzymes, and lipids.
11. The system of claim 7 wherein said cellular target is an enzyme.
12. The system of claim 7 wherein said cellular target is hexokinase.
13. The system of claim 1 wherein said imaging agent accumulates in malignant tissue at a different rate than in non-malignant tissue.
14. The system of claim 1 wherein said imaging agent accumulates in abnormal myocardial tissue at a different rate than in normal myocardial tissue.
15. The system of claim 1 wherein said imaging agent is non-radioactive and has a logP of above 0.0.
16. A system for radiographic imaging of body tissue comprising:
  - a) a radio-opaque imaging agent which is capable of entering a cell through passive diffusion and which selectively binds to a cellular target;
  - b) means for administering said imaging agent to a patient;
  - c) means for generating an X-ray beam; and
  - d) means for acquiring radiographic images disposed on the side of said patient opposite said X-ray beam generating means.

17. The system according to claim 16, wherein the means for generating said X-ray beam is capable of generating a plurality of beams with predetermined different energy spectra and further comprising means for performing a weighted combination of a plurality of said radiographic images to produce a single image.
18. The system of claim 17 wherein said plurality of beams are quasi-monoenergetic.
19. The system of claim 17 wherein said plurality of beams are monoenergetic.
20. The system of claim 17 wherein 2 beams are generated.
21. The system of claim 17 wherein more than 2 beams are generated.
22. The system of claim 17 wherein said means for generating said plurality of beams with predetermined different energy spectra is disposed between said means for generating an X-ray beam and said patient.
23. The system of claim 17 wherein said means for generating said plurality of beams with predetermined different energy spectra is disposed between said patient and said means for acquiring radiographic images.
24. The system of claim 17, further including means for displaying variable proportions of radiographic density contributed by said imaging agent, soft tissue, and bone to said single image.

25. The system of claim 16 wherein said cellular target is a cellular structure.
26. The system of claim 16 wherein said cellular target is a molecule.
27. The system of claim 16 wherein said cellular target is selected from the group of proteins, nucleic acids, coenzymes, and lipids.
28. The system of claim 16 wherein said cellular target is an enzyme.
29. The system of claim 16 wherein said cellular target is hexokinase.
30. The system of claim 16 wherein said imaging agent accumulates in malignant tissue at a different rate than in non-malignant tissue.
31. The system of claim 16 wherein said imaging agent accumulates in abnormal myocardial tissue at a different rate than in normal myocardial tissue.
32. The system of claim 16 wherein said imaging agent is non-radioactive and has a logP of above 0.0.
33. A method for radiographic imaging of body tissue comprising:
- a) administering to a live organism a bidirectionally cell membrane-permeable, radio-opaque imaging agent;
  - b) generating an X-ray beam;
  - c) illuminating said tissue with said X-ray beam; and
  - d) acquiring a radiographic image of said tissue during illumination.
34. The method of claim 33, further including:

- a) generating a plurality of X-ray beams with predetermined different energy spectra;
  - b) illuminating said tissue with each of said plurality of beams;
  - c) acquiring a radiographic image of said tissue during illumination by each of said plurality of beams; and
  - d) performing a weighted combination of a plurality of said radiographic images to produce a single image.
35. The method of claim 34 wherein said plurality of beams are monoenergetic.
36. The method of claim 34 wherein said plurality of beams are quasi-monoenergetic.
37. The system of claim 34 wherein 2 beams are generated.
38. The system of claim 34 wherein more than 2 beams are generated.
39. The method of claim 34, further displaying variable proportions of radiographic density contributed by said imaging agent, soft tissue, and bone to said single image.
40. The method of claim 33 wherein said cell membrane-permeable, radio-opaque imaging agent selectively binds to a cellular target.
41. The method of claim 40 wherein said cellular target is a cellular structure.
42. The method of claim 40 wherein said cellular target is a molecule.

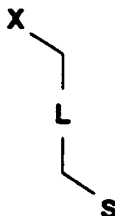
43. The method of claim 40 wherein said cellular target is selected from the group of proteins, nucleic acids, coenzymes, and lipids.
44. The method of claim 40 wherein said cellular target is an enzyme.
45. The method of claim 40 wherein said cellular target is hexokinase.
46. The method of claim 33 wherein said imaging agent accumulates in malignant tissue at a different rate than in non-malignant tissue.
47. The method of claim 33 wherein said imaging agent is non-radioactive and has a logP of above 0.0.
48. A method for radiographic imaging of body tissue comprising:
- a) administering to a live organism a cell membrane-permeable, radio-opaque imaging agent which selectively binds to an intracellular target in the organism;
  - b) generating an X-ray beam;
  - c) illuminating said tissue with said X-ray beam; and
  - d) acquiring a radiographic image of said tissue during illumination.
49. The method of claim 48, further including:
- a) generating a plurality of X-ray beams with predetermined different energy spectra;
  - b) illuminating said tissue with each of said plurality of beams;
  - c) acquiring a radiographic image of said tissue during illumination by each of said plurality of beams; and

- d) performing a weighted combination of a plurality of said radiographic images to produce a single image.
50. The method of claim 49 wherein said plurality of beams are monoenergetic.
51. The method of claim 49 wherein said plurality of beams are quasi-monoenergetic.
52. The system of claim 49 wherein 2 beams are generated.
53. The system of claim 49 wherein more than 2 beams are generated.
54. The method of claim 49, further displaying variable proportions of radiographic density contributed by said imaging agent, soft tissue, and bone to said single image.
55. The method of claim 48 wherein said intracellular target is a cellular structure.
56. The method of claim 48 wherein said intracellular target is a molecule.
57. The method of claim 48 wherein said intracellular target is selected from the group consisting of proteins, nucleic acids, coenzymes, and lipids.
58. The method of claim 48 wherein said intracellular target is an enzyme.
59. The method of claim 48 wherein said intracellular target is hexokinase.
60. The method of claim 48 wherein said imaging agent accumulates in malignant tissue at a different rate than in non-malignant tissue.

61. The system of claim 48 wherein said imaging agent accumulates in abnormal myocardial tissue at a different rate than in normal myocardial tissue.
62. The method of claim 48 wherein said imaging agent is non-radioactive and has a logP of above 0.0.
63. A method for generating a functional image and an anatomical image of tissue in registration comprising:
- a) administering to a live organism a radio-opaque imaging agent;
  - b) generating a plurality of X-ray beams with predetermined different energy spectra;
  - c) illuminating said tissue with each of said plurality of beams;
  - d) acquiring a radiographic image of said tissue during illumination by each of said plurality of beams;
  - e) generating said functional image from at least two of said radiographic images.
64. The method of claim 63 wherein said radio-opaque imaging agent comprises a composition having a general formula S-L-X, wherein said composition is cell membrane-permeable and wherein:
- S is a binding moiety which selectively binds to a cellular molecule;
- X is a radio-opaque moiety; and
- L is a linking moiety which links the S moiety to the X moiety.



65. A composition having the general formula



wherein:

the S moiety is a pyranose or a furanose;

the X moiety is an unsubstituted or substituted  $C_1-C_8$  alkyl, alkoxy, alkylthio, alkenyl, alkylaryl, alkylamino, alkylamido, amido, or arylamido, in which at least one atom is substituted by a radio-opacifying atom of an element with an atomic number of approximately  $Z = 35$  to approximately  $Z = 74$ ; and

the L moiety is an unsubstituted or substituted  $C_1-C_8$  alkyl, alkoxy, alkylthio, alkenyl, alkylaryl, alkylamino, alkylamido, amido, or arylamido, bonded to the S moiety and to the X moiety.

66. The composition of claim 65 wherein the S moiety is hydroxy-substituted.

67. The composition of claim 65 wherein the S moiety is 2-hydroxy-substituted.

68. The composition of claim 65 wherein:

the S moiety is a substituted pyranose of the formula  $C_6H_{11}O_5$ ,

the X moiety is a substituted aryl of the formula  $C_6H_2I_3$ , and

the L moiety is a substituted amidoaryl of the formula  $C_6H_3NH_2NHCO$ .

69. The composition of claim 65 wherein:

the S moiety is a substituted pyranose of the formula  $C_6H_{11}O_5$ ,

the X moiety is a substituted aryl of the formula  $C_6Hl_3CH_2CH_3$ , and

the L moiety is a substituted amidoaryl of the formula  $C_6H_3NH_2NHCO$ .

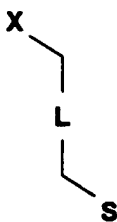
70. The composition of claim 65 wherein:

the S moiety is a substituted pyranose of the formula  $C_6H_{11}O_5$ ,

the X moiety is a substituted aryl of the formula  $C_6I_3(CONHCH_3)_2$ , and

the L moiety is a substituted amidoaryl of the formula  $C_6H_3NH_2NHCO$ .

71. A composition having the general formula



wherein:

the S moiety is an oligonucleotide in which the nucleotide sequence comprises at least two residues;

the X moiety is an unsubstituted or substituted  $C_1-C_8$  alkyl, alkoxy, alkylthio, alkenyl, alkylaryl, alkylamino, alkylamido, amido, or arylamido, in which at least one atom is substituted by a radio-opacifying atom of an element with an atomic number of approximately  $Z = 35$  to approximately  $Z = 74$ ; and

the L moiety is an unsubstituted or substituted  $C_1-C_8$  alkyl, alkoxy, alkylthio, alkenyl, alkylaryl, alkylamino, alkylamido, amido, or arylamido, bonded to the S moiety and to the X moiety.

72. The composition of claim 71 wherein the internucleotide linkage is nonionic.

73. The composition of claim 71 wherein one or more lipophilic groups is bonded to at least one of the group consisting of the S moiety, the X moiety, and the L moiety.

74. A composition which is cell membrane-permeable and radio-opaque and has a logP of above 0.0.

75. The composition of claim 74 which further selectively binds to a cellular target.

76. A method of imaging tissue comprising:

a) administering a composition having a general formula S-L-X, wherein said composition is cell membrane-permeable and wherein:

S is a binding moiety which selectively binds to a cellular molecule in said tissue;

X is a radio-opaque moiety; and

L is a linking moiety which links the S moiety to the X moiety;

b) irradiating said tissue with a radiation source which is capable of being attenuated by the X moiety; and

c) acquiring an image of said tissue.

77. The method of claim 76 wherein said acquiring occurs during said irradiating and wherein said composition is non-radioactive and wherein said tissue is in vivo.

78. The method of claim 76 further comprising determining whether said tissue comprises malignant tissue using said image.

79. The method of claim 76 further comprising determining whether said tissue comprises abnormal myocardial tissue using said image.

80. A computer-readable storage medium containing executable computer instructions which, when executed by a digital image processing system, cause said digital image processing system to perform a method comprising:

- a) acquiring a plurality of radiographic images, wherein each of said radiographic images is acquired during transillumination of tissue in a living organism by one of a plurality of X-ray beams with a predetermined unique energy spectrum, said living organism having been administered a radio-opaque imaging agent; and
- b) generating a functional image from said plurality of radiographic images.

81. A computer-readable storage medium as in claim 80 wherein said method further comprises:

- a) displaying said functional image; and
- b) displaying one of said plurality of radiographic images which is an anatomical image.

82. A computer-readable storage medium as in claim 81 wherein said functional image and said anatomical image are displayed simultaneously and in aligned registration.

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83. A computer-readable storage medium as in claim 81 wherein said functional image and said anatomical image are displayed separately.
84. A computer-readable storage medium containing executable computer program instructions which, when executed by a digital image processing system, cause said digital image processing system to perform a method comprising:
- a) acquiring at least one radiographic image obtained by irradiating tissue in a living organism with a radiation source which is capable of being attenuated by a composition which is administered to said living organism, wherein said composition is bidirectionally cell membrane-permeable and radio-opaque and capable of binding to a cellular target; and
  - b) generating an image from at least one of said radiographic images.
85. A computer-readable storage medium as in claim 84 wherein said method further comprises displaying said image which is a functional image.
86. A computer-readable storage medium as in claim 84 wherein said method further comprises displaying a radiographic image which is an anatomical image and which is in registration with said functional image.